

active binding compounds with optimal spacing between the binding site moieties may enhance binding site interactions. See e.g. Lee et al., (1984) *Biochem.* 23:4255. The artisan may control the multivalency and spacing by selection of a suitable carrier moiety or linker units. Useful moieties include molecular supports comprising a multiplicity of functional groups that can be reacted with functional groups associated with the active compounds of the invention. A variety of carrier moieties may be used to build highly active multimers, including proteins such as BSA (bovine serum albumin), peptides such as pentapeptides, decapeptides, pentadecapeptides, and the like, as well as non-biological compounds selected for their beneficial effects on absorbability, transport, and persistence within the target organism. Functional groups on the carrier moiety, such as amino, sulfhydryl, hydroxyl, and alkylamino groups, may be selected to obtain stable linkages to the compounds of the invention, optimal spacing between the immobilized compounds, and optimal biological properties.

[0153] “A pharmaceutically acceptable prodrug” is a compound that may be converted under physiological conditions or by solvolysis to the specified compound or to a pharmaceutically acceptable salt of such compound, or a compound that is biologically active with respect to the intended pharmacodynamic effect. “A pharmaceutically active metabolite” is intended to mean a pharmacologically active product produced through metabolism in the body of a specified compound or salt thereof. Prodrugs and active metabolites of a compound may be identified using routine techniques known in the art. See, e.g., Bertolini, G. et al., (1997) *J. Med. Chem.* 40:2011-2016; Shan, D. et al., *J. Pharm. Sci.*, 86(7):765-767; Bagshawe K., (1995) *Drug Dev. Res.* 34:220-230; Bodor, N., (1984) *Advances in Drug Res.* 13:224-331; Bundgaard, H., *Design of Prodrugs* (Elsevier Press, 1985); and Larsen, I. K., *Design and Application of Prodrugs*, Drug Design and Development (Krogsgaard-Larsen et al., eds., Harwood Academic Publishers, 1991).

[0154] If the compound of the present invention is a base, the desired pharmaceutically acceptable salt may be prepared by any suitable method available in the art, for example, treatment of the free base with an inorganic acid, such as hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid and the like, or with an organic acid, such as acetic acid, maleic acid, succinic acid, mandelic acid, fumaric acid, malonic acid, pyruvic acid, oxalic acid, glycolic acid, salicylic acid, a pyranosidyl acid, such as glucuronic acid or galacturonic acid, an α -hydroxy acid, such as citric acid or tartaric acid, an amino acid, such as aspartic acid or glutamic acid, an aromatic acid, such as benzoic acid or cinnamic acid, a sulfonic acid, such as p-toluenesulfonic acid or ethanesulfonic acid, or the like.

[0155] If the compound of the present invention is an acid, the desired pharmaceutically acceptable salt may be prepared by any suitable method, for example, treatment of the free acid with an inorganic or organic base, such as an amine (primary, secondary or tertiary), an alkali metal hydroxide or alkaline earth metal hydroxide, or the like. Illustrative examples of suitable salts include organic salts derived from basic amino acids, such as lysine and arginine, ammonia, primary, secondary, and tertiary amines, and cyclic amines, such as piperidine, morpholine and piperazine, and inorganic salts derived from sodium, calcium, potassium, magnesium, manganese, iron, copper, zinc, aluminum and lithium.

[0156] In the case of compounds that are solids, it is understood by those skilled in the art that the compound of the present invention and salts may exist in different crystal or polymorphic forms, all of which are intended to be within the scope of the present invention and specified structural formulas.

[0157] The compounds of the present invention are useful in inhibiting BoNT/A LC metalloprotease activity. The compounds of the present invention are also useful in treating, inhibiting or preventing intoxication caused by botulinum toxin in a subject. Further, since some of the compounds of the present invention are found to exhibit antibacterial activity, the compounds of the present invention are useful in inhibiting, reducing or preventing growth of or destroying bacteria of at least one bacterial strain.

[0158] The compounds of the present invention are also useful in treating, inhibiting or preventing an infection caused by bacterial of at least one bacterial strain in a subject. The bacteria belong to various gram positive and gram negative bacteria strains including *Bacillus*, *Burkholderia*, *Enterobacter*, *Escherichia*, *Helicobacter*, *Klebsiella*, *Mycobacterium*, *Neisseria*, *Pseudomonas*, *Staphylococcus*, *Streptococcus*, *Yersinia* and the like, including drug resistance strains. In preferred embodiments, the bacteria is *B. anthracis* (including Ames strain and ciprofloxacin resistant Ames strain) *B. anth1024*, *B. brevis*, *B. licheniformis*, *B. megaterium*, *B. pumilus*, *B. subtilis*, *B. vollum*, and spores thereof; *B. cepacia*, *B. mallei*, *M. pseudomallei*, and *B. thailandensis*; *E. coli*, *E. faecalis*, *E. faecium*, and vancomycin resistant strains thereof; *K. pneumoniae*; *P. aeruginosa*, preferably PAO1; *S. aureus* and methicillin resistant *S. aureus*; *Y. pestis*; or a combination thereof.

[0159] The activity of the compounds of the present invention may be measured by any of the methods available to those skilled in the art, including in vitro and in vivo assays. Examples of suitable assays for activity measurements are provided herein. Properties of the compounds of the present invention may be assessed, for example, by using one or more of the assays set out in the Examples below. Other pharmacological methods may also be used to determine the efficacy of the compounds a subject suffering from a given disease or disorder. The compounds of the present invention may be used in combination with or as a substitution for treatments known in the art.

[0160] The therapeutically effective amounts of the compounds of the invention for treating the diseases or disorders described above in a subject can be determined in a variety of ways known to those of ordinary skill in the art, e.g. by administering various amounts of a particular compound to a subject afflicted with a particular condition and then determining the effect on the subject. Typically, therapeutically effective amounts of a compound of the present invention can be orally administered daily at a dosage of the active ingredient of 0.002 to 200 mg/kg of body weight. Ordinarily, a dose of 0.01 to 10 mg/kg in divided doses one to four times a day, or in sustained release formulation will be effective in obtaining the desired pharmacological effect. It will be understood, however, that the specific dose levels for any particular subject will depend upon a variety of factors including the activity of the specific compound employed, the age, body weight, general health, sex, diet, time of administration, route of administration, and rate of excretion, drug combination and the severity of the particular disease.